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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,693	01/26/2001	Steven V. Beer	19603/2501 (CRF D-2375A)	6816

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Michael L. Goldman
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603

EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 03/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/770,693

Applicant(s)

BEER ET AL.

Examiner

Anne R. Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 9, 10, 14, 15, 17, 18, 20-28, 30-33, 35-40, 43, 44, 48, 49, 51, 52, 54-62, 64-69 and 71-78 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims:

Claims pending in the application are 1-4,9,10,14,15,17,18,20-28,30-33,35-40,43,44,48,49,51,52,54-62,64-69 and 71-78.

DETAILED ACTION

1. Claims 1-4, 9-10, 14-15, 17-18, 20-28, 30-33, 35-40, 43-44, 48-49, 51-52, 54-62, 64-69 and 71-78 are pending.
2. In light of Applicant statement that use of one DNA encoding a hypersensitive response elicitor would be obvious over use of another, the restriction among the groups is withdrawn and all claims are examined.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The objection to claims 14-15, 17-18, 20-21, 48-49, 51-52 and 54-55 because of informalities is withdrawn in light of Applicant's amendment of the claims.
5. The rejection of claims 1, 7-27, 30, 35-61 and 64-72 under 35 U.S.C. 103(a) as being unpatentable over Bauer et al (1998, US 5,850,015) in view of each of Doerner et al (1990, Bio/Technol. 8:845-848) and Kawamata et al (1997, Plant Cell Physiol. 38:792-803) is withdrawn in light of Applicant's amendment of the claims.
6. The rejection of claims 2-4, 28, 31-33 and 62 under 35 U.S.C. 103(a) as being unpatentable over Bauer et al in view of each of Doerner et al and Kawamata et al as applied to claims 1, 7-27, 30, 35-61 and 64-72 above, and further in view of Gopalan et al (1996, Plant Cell, 8:1095-1105) is withdrawn in light of Applicant's amendment of the claims.
7. The rejection of claims 1-2, 7-28, 30-31, 35-44, 56-62 and 64-72 under 35 U.S.C. 103(a) as being unpatentable over Chappell et al (US Patent 5,981,843, filed May, 1995) in view of Zitter et al (US Patent 5,977,060, filed February 1997) is withdrawn in light of Applicant's amendment of the claims.

Claim Objections

8. Claims 35, 38, 40, 64, 67 and 69 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claimed plants would inherently be resistant to the listed oomycete species, and the claimed methods would inherently produce plants with resistance to those oomycete species; thus the claims fail to limit the parent claims. The objection is repeated for the reasons of record as set forth in the Office action mailed 27 May 2004. Applicant's arguments filed 1 December 2004 have been fully considered but they are not persuasive.

Applicant urges that the claims contain a Markush group reciting different oomycete genera, and it limits "oomycete" in the independent claim (response pg 10).

This is not found persuasive. The listing of oomycete genera would only limit the claims if some hypersensitive response elicitor provided resistance to some oomycetes and not others.

Claim Rejections - 35 USC § 112

9. Claims 1-4, 9-10, 14-15, 17-18, 20-28, 30-33, 35-40, 43-44, 48-49, 51-52, 54-62, 64-69 and 71-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chimeric genes encoding SEQ ID NOs: 1, 3, 5 or 7 operably linked to the *gstI* promoter, with a secretion signal sequence, cells transformed with the construct, and oomycete-resistant plants transformed with the construct, does not reasonably provide enablement for

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constructs comprising any hypersensitive response elicitor-encoding nucleic acid, including those that hybridize to SEQ ID NO:2, 4, 6 or 8 operably linked to any promoter that is activated by an oomycete or cells and plants transformed with those constructs, or for constructs without a nucleic acid encoding a secretion signal peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 27 May 2004, as applied to claims 1-73, due to Applicant's amendment of the claims. Applicant's arguments filed 1 December 2004 have been fully considered but they are not persuasive.

The claims are broadly drawn to constructs comprising any hypersensitive response elicitor-encoding nucleic acid, including those that hybridize to SEQ ID NO:2, 4, 6 or 8 operably linked to any promoter that is activated by an oomycete or cells and plants transformed with those constructs, or for constructs without a nucleic acid encoding a secretion signal peptide, expression systems, cells, and plants comprising the chimeric gene, and a method of making a plant resistant to disease by transformation with the chimeric gene.

The instant specification, however, only provides guidance for the cloning of PCR amplification products of the *gstI* (*prpI*) promoter (SEQ ID NO:9) from potato, comparison of the sequences of the clones to the published sequence, and construction of *gstI:uidA* constructs (example 1); *Agrobacterium*-mediated transformation of *Arabidopsis* with the constructs, inoculation of the transformed plants with *Peronospora parasitica* or *Pseudomonas syringae* pv *tomato* to show that the promoter induces expression in response to an oomycete and not to a bacteria (example 2), transformation of *Arabidopsis* with *gstI:hrpN* or *gstI*:secretion signal

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sequence:*hrpN* constructs and testing of the transgenic plants for resistance to *P. parasitica* - plants with the *gstI*:secretion signal sequence:*hrpN* construct were reported to be resistant, while the resistance status of plants transformed with the *gstI*: *hrpN* construct were not reported (example 3). The only hypersensitive response elicitors taught in the specification were SEQ ID NOs:2, 4, 6 and 8 from each of *E. chrysanthemi*, *E. amylovora*, *P. syringae*s and *P. solanacearum*, respectively.

The instant specification fails to provide guidance for where to find nucleic acids encoding hypersensitive response elicitors within the full scope of the claims and it does not provide guidance for how to make them.

Expression of hypersensitive response elicitors that are not linked to secretion signal peptides do not produce pathogen resistant plants. Bauer et al (1999, Acta Hort. 489:301-304) transformed *Arabidopsis* plants with the *hrpN* gene expressed behind the *gstI* promoter and showed that the *hrpN* construct must be expressed with a signal sequence for export of the protein from the plants cells for production of resistant plants to be successful (pg 302, paragraph 5). Elicitors must be exported to the outside of the cell for functional interaction with membrane bound binding sites of the plant (Keller et al, 1999, Plant Cell 11:223-235, see pg 224, right column, paragraph 4; see also Bauer et al, pg 302, paragraph 6). The instant specification fails to teach the necessity for signal sequences for protein export.

Given the claim breath and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

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Applicant urges that Bauer only teaches that a secretion signal afforded the best results, but that without one the construct functioned to reduce the severity of an onset of infection (response pg 10-11).

This is not found persuasive because the method of claims 58-61, 64-69 and 77 is one of making a plant resistant to oomycete infection. Plants transformed with constructs without the secretion signal were not resistant to infection.

Applicant urges that one of skill in the art is fully able to identify other nucleic acids encoding hypersensitive response elicitors and use them in the claimed methods (response pg 11).

This is not found persuasive because the specification does not provide specific guidance for how to find and how to make the claimed nucleic acids.

10. Claims 1-4, 22-28, 30-33, 35-40, 56-62, 64-69 and 71-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 27 May 2004, as applied to claims 1-73. Applicant's arguments filed 1 December 2004 have been fully considered but they are not persuasive.

Applicant urges that written description violations cannot be based upon genus size alone (response pg 11-12).

This is not found persuasive. The four HRE genes described in the specification do not describe the full scope of the HRE genes used in the claimed constructs, plants and methods.

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Applicant urges that the specification teaches the elicitors found after the filing date of the instant application can be used to practice the invention and that each species need not be described (response pg 12).

This is not found persuasive. Three hypersensitive response elicitors found after the filing date of the instant application have structural and functional features that are very different from the four hypersensitive response elicitors described in the specification. Kim et al (1998, J. Bacteriol. 180:5203-5210) teach that HrpW is not homologous to any harpins and that it comprises a pectin-lyase-like domain (pg 5205, right column, paragraph 1). The dspE protein functions as an avirulence protein hypersensitive response elicitor (Bogdanove et al, 2001, US Patent 6,228,644; column 35, line 30, to column 37, line 25). The dspF protein is structurally similar to a chaperone and only 4 of its 139 amino acids are glycines (Bogdanove et al, SEQ ID NO:4; column 37, lines 30-41). These structural and functional features of hypersensitive response elicitors are not described by the specification.

Applicant urges that they demonstrated in the Wei Declaration that bacterial hypersensitive response elicitors are an art-recognized class, and resummaries the Declaration (response pg 12-14).

This is not found persuasive. Hypersensitive response elicitors have structural and functional features that are very different from the four hypersensitive response elicitors described in the specification.

Applicant urges that the Office did not demonstrate that the genus contains structurally and functionally unrelated species (response pg 14).

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This is not found persuasive. Kim et al (1998, J. Bacteriol. 180:5203-5210) teach that HrpW is not homologous to any harpins and that it comprises a pectin-lyase-like domain (pg 5205, right column, paragraph 1). The dspE protein functions as an avirulence protein hypersensitive response elicitor (Bogdanove et al, 2001, US Patent 6,228,644; column 35, line 30, to column 37, line 25). The dspF protein is structurally similar to a chaperone and only 4 of its 139 amino acids are glycines (Bogdanove et al, SEQ ID NO:4; column 37, lines 30-41). These structural and functional features of hypersensitive response elicitors are not described by the specification.

11. Claims 73-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 27 May 2004, as applied to claims 1-73. Applicant's arguments filed 1 December 2004 have been fully considered but they are not persuasive.

The term "glycine rich" in claim 73 is a relative term that renders the claim indefinite. The term "glycine rich" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. How many or what proportion of glycine distinguishes a glycine rich protein from one that is not?

Applicant urges that numerous references use the term to describe hypersensitive response elicitors; thus those of skill in the art appreciate this term (response pg 14-15).

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This is not found persuasive. What one person considers glycine-rich may not be considered glycine-rich by another. The metes and bounds of the claims are unclear because the cutoff for a protein being “glycine-rich” or not being “glycine-rich” is unclear.

The term “substantially no cysteine” in claim 73 is a relative term that renders the claim indefinite. The term “substantially no cysteine” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant urges that most definitions of this class of hypersensitive response elicitors use the term “lacks cysteine” but the instant claims encompass the possibility that a cysteine may be present (response pg 15).

This is not found persuasive. It is not clear how many or what proportion of cysteine distinguishes a protein with substantially no cysteine from one that has a substantial number of cysteines.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

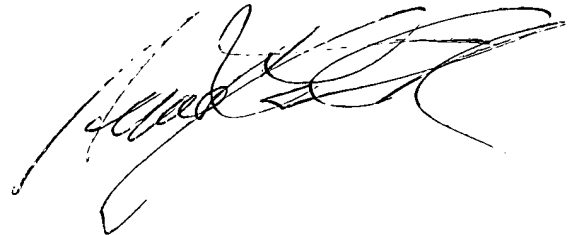
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne R. Kubelik, Ph.D.
February 25, 2005

A handwritten signature in black ink, appearing to read 'Anne R. Kubelik', with a stylized flourish at the end.

**ANNE KUBELIK, PH.D.
PRIMARY EXAMINER**